PrEP Overview for Providers

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www.hepatitis.va.gov

Background

Nearly 50,000 new HIV infections in the United States are diagnosed every year, and this number has changed little in the past 5 years. VHA is the nation's largest single HIV care provider.

PrEP, or pre-exposure prophylaxis, is a tool for reducing HIV risk in appropriate persons; it can and should be used with other HIV prevention methods. The combination of tenofovir/emtricitabine (TDF/FTC, Truvada®) was approved by the U.S. Food and Drug Administration in 2012 for use "in combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk." TDF/FTC also is used as PrEP for injection drug users (IDUs). The CDC recommends PrEP for HIV-uninfected persons with "substantial risk" of HIV. VHA supports the use of PrEP and follows CDC guidelines.

Truvada® is dosed as 1 pill orally once daily (TDF 300 mg/FTC 200 mg).

Efficacy and Safety

Clinical studies have evaluated the efficacy and safety of PrEP (either oral tenofovir/emtricitabine or oral tenofovir alone) in heterosexually active men and women, men who have sex with men (MSM), transgender (TG) women who have sex with men, and IDUs.

- Among MSM and TG women who have sex with men, PrEP (TDF/FTC) reduced overall relative risk of HIV infection by 44%, but the risk reduction was more than 90% among those with the highest rates of adherence.
- In heterosexual HIV-discordant couples, TDF/FTC was 75% effective overall in reducing HIV transmission to the uninfected partner, and 90% effective in those with the highest levels of adherence.
- In heterosexual single women and men, TDF/FTC PrEP reduced HIV infection rates by 62-85%, with efficacy again closely related to adherence.
- In IDUs, use of oral TDF as PrEP was associated with a 49% reduction in HIV infection.

In all these studies, *higher rates of adherence to PrEP were strongly associated with better efficacy*. And in all studies, participants were encouraged to use additional prevention methods concurrently.

Side effects of TDF/FTC when used as PrEP include GI symptoms (nausea, diarrhea, abdominal discomfort) and headache. These were relatively uncommon and usually resolved within weeks of PrEP initiation. Renal dysfunction and bone loss have been reported.

For patients who become infected with HIV while on TDF/FTC or those who are infected at the time PrEP was initiated, viral resistance to the PrEP drugs may occur.

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Target Populations for PrEP

Consider PrEP for individuals who are at substantial risk of HIV acquisition, including:

- Sexually active MSM
- Heterosexually active women and men
- Transgender women and men
- Adult IDUs
- Heterosexually active women and men whose partners are known to have HIV infection

Substantial risk includes:

- Using condoms inconsistently
- Having a high number of sex partners
- Having an HIV-positive sex partner
- Recently acquiring a sexually transmitted disease (STD)
- Having an HIV-infected injecting partner
- Sharing injection or drug preparation equipment
- Engaging in commercial sex work

Note that this group includes a broad segment of the population.

Screening Patients for PrEP

A clinic visit to evaluate the suitability of PrEP includes history, lab tests, and careful education and counseling about PrEP, as indicated below.

- History should include a thorough review of current/recent sex and drug-use behaviors, an assessment of any symptoms consistent with acute HIV infection, and intentions for pregnancy.

  Of course, it is important to be open and nonjudgmental in order to have full and frank conversations about sex and drug-use behaviors (see Appendix).

- HIV infection must be ruled out before PrEP is given:
  - HIV testing should be done with a 4th-generation Ag/Ab test if possible, because these are most sensitive to acute/recent HIV infection; oral rapid tests are not recommended.
  - HIV testing should be done within 1 week before PrEP initiation.
  - If the HIV test result is negative or indeterminate, assess for the possibility of current acute HIV infection (with a false-negative HIV result): ask about symptoms and history of risky exposures. Consider ordering an HIV PCR assay to rule out acute infection.

- Hepatitis B status must be assessed.
    - If negative for evidence of infection or immunity: vaccinate.
    - If positive: consult with an HIV or HBV specialist before initiating PrEP; both TDF and FTC are active against hepatitis, B and special considerations apply. For further information on HBV, see http://www.hepatitis.va.gov/.
- Renal impairment should be ruled out. TDF/FTC PrEP should not be given to persons with creatinine clearance (CrCl) less than 60 mL/min.
- Mental health issues should be assessed. Refer for mental health or substance-use care if indicated.
- Consider consultation with an HIV or Infectious Disease clinician.
- Patients should be educated about symptoms of acute HIV infection and told to call immediately if these develop.

Signs and Symptoms of Acute HIV Infection

Fever	Headache	Arthralgia
Fatigue	Adenopathy	Diarrhea
Myalgia	Night sweats	Rash
Pharyngitis		

Prescribing PrEP

- TDF/FTC should be prescribed as 1 pill orally once daily.
- VHA recommends giving a 90-day supply, but no refills should be included – it is important to reassess the PrEP patient's HIV status and other factors before a new prescription is given (see below).

It may take days or even a couple of weeks before TDF and FTC levels are protective; advise patients to be particularly attentive to condom use in this period.

Follow-Up

PrEP patients should be seen and reevaluated at least every 3 months; each reevaluation should include history, lab evaluation, and education and counseling. History should include an assessment of adherence to TDF/FTC, side effects, symptoms of acute HIV infection, and interval sex and drug-use risks. Testing for HIV (as well as renal function and STDs) should be done, and counseling and support for adherence and HIV risk-reduction behaviors should be provided (see table below). It is important to reinforce both the potential benefits and limitations of PrEP.

At each visit, the decision about whether to continue PrEP should be based on results of HIV and safety tests, adverse effects, adherence, and ongoing risks of HIV infection.

Components of PrEP Screening and Follow-Up Visits

History	Lab Evaluation	Counseling/Education
All visits: ▪ HIV risk behaviors ▪ Substance-use and alcohol-use behaviors ▪ Symptoms or recent history of STDs ▪ Symptoms of acute HIV ▪ Mental health screening ▪ Adherence to other medications **Follow-up visits:** ▪ Adherence to PrEP	**All visits:** ▪ HIV test ▪ Pregnancy test (women) ▪ Creatinine (every 3-6 months) ▪ STD tests: syphilis, gonorrhea, chlamydia, and (in women) trichomoniasis (every 3-6 months and as indicated) **Initial visit:** ▪ Hepatitis B serology AG (sAb, cAb)	**All visits:** ▪ Risk-reduction counseling ▪ Education about TDF/FTC: potential benefits, risks, and adverse effects ▪ Emphasis upon need for follow-up every 3 months ▪ Referral for mental/ behavioral health or substance-use intervention as indicated **Follow-up visits:** ▪ Reassess need for PrEP (at least yearly)

If a decision is made to stop PrEP (e.g., if the person's risk decreases, if side effects are not tolerable, or in the case of poor adherence), it generally is best to continue for 28 days beyond the last risky exposure. If the patient has hepatitis B, consult with a specialist before stopping TDF/FTC – a flare of hepatitis B may occur. Document the patient's HIV status, reason for discontinuation, recent adherence, and recent risk behaviors.

If patient tests positive for HIV: stop PrEP immediately, and refer the patient urgently for HIV care. TDF/FTC is not adequate to treat HIV infection, and the virus may develop resistance to one or both of the drugs if PrEP is continued. It is important to counsel the patient on reducing the risk of transmitting HIV (e.g., by condom use), particularly as the early stages of HIV infection are highly infectious.

Resources and References

Clinician Consultation Center – clinically supported telephone consultation on pre-exposure prophylaxis (PrEP) for VA health care providers available at 855-448-7737; Monday-Friday, 11 a.m. – 6 p.m. (EST).

United States Public Health Service; U.S. Centers for Disease Control and Prevention; National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. *Preexposure Prophylaxis for the Prevention of HIV Infection – 2014: A Clinical Practice Guideline*. May 14, 2014. Available at http://aidsinfo.nih.gov/guidelines.

United States Public Health Service; U.S. Centers for Disease Control and Prevention; National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. *Preexposure Prophylaxis for the Prevention of HIV Infection – 2014: Clinical Providers' Supplement*. May 14, 2014. Available at http://aidsinfo.nih.gov/guidelines.

Appendix

Elements of Brief HIV Risk-Reduction Counseling in Clinical Settings
• Create and maintain a trusting and confidential environment for discussion of sexual or substance abuse behaviors. • Build an ongoing dialogue with patients regarding their risk behavior (and document presence or absence of risk behaviors in the confidential medical record). • Reinforce the fact that PrEP is not always effective in preventing HIV infection, particularly if used inconsistently, but that consistent use of PrEP together with other prevention methods (consistent condom use, discontinuation of drug injection use or never sharing injection equipment) confers very high levels of protection.

Source: U.S. Public Health Service; U.S. Centers for Disease Control and Prevention; National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. *Preexposure Prophylaxis for the Prevention of HIV Infection – 2014: Clinical Providers' Supplement*. May 14, 2014. Available at http://aidsinfo.nih.gov/guidelines.